

Dose Supplemental Zinc Prevents Recurrence of Febrile Seizures?

How to Cite this Article: Shiva S, Barzegar M, Zokaie N, Shiva Sh. Dose Supplemental Zinc Prevents Recurrence of Febrile Seizures? Iranian Journal of Child Neurology 2011;5(4):11-14.

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Received: 21-Jun- 2011

Last Revised: 14 -Sep- 2011

Accepted: 21 -Sep- 2011

Abstract

Objective

Febrile seizures (FS) are the most common form of seizures in children. Previous studies have suggested that zinc may play a role in the prevention of FS. However, there is limited information on the preventative effects of zinc against FS. This study aimed to determine whether prescribing zinc supplements could prevent FS.

Materials & Methods

In a randomized, placebo-controlled trial, 100 children who had experienced simple FS for the first time were recruited. Children in the case group (50 patients) were orally administered 1mg/kg/day zinc sulfate for 1 year, and children in the control group (50 patients) received a placebo. Serum zinc levels in both the control and case groups were measured at the start and at the end of the study, and recurrent cases of FS were recorded.

Results

The case group consisted of 29 boys (58%) and 21 girls (42%) with a mean age of 2.06 ± 0.83 , and the control group consisted of 31 boys (62%) and 19 girls (38%) with a mean age of 2.22 ± 1.04 years. An inverse relationship was found between febrile diseases and serum zinc levels. In other words, the occurrence of febrile diseases decreased with an increase in serum zinc levels. Eight children (16%) in the case group and 8 in the control group experienced recurrent FS within a year.

Conclusion

Supplemental doses of zinc (1mg/kg/day) reduced the rate of febrile illnesses, but did not prevent the recurrence of FS.

Keywords: Seizures; febrile; child; prevention and control

Introduction

A seizure is a paroxysmal event caused by abnormal electrical discharge inside the brain (1). The exact pathogenesis of seizures is not fully understood but involves several factors such as genetic predisposition and, changes in the levels of neurotransmitters and some trace elements (2). Febrile seizures (FS) are the most common form of seizures and are twice as common in boys as in girls (1, 3). FS are triggered when patients with a low seizure threshold develop a fever (4). Risk factors for FS include genetic factors, micronutrient deficiencies (e.g., iron, zinc), and immunologic reactions. Zinc is an important micronutrient and trace element that plays important roles in growth and development, immune

system response, neurological function, nerve impulse transmission, and hormone release (5, 6). The levels of gamma-amino-butyric acid (GABA), which is the major inhibitory neurotransmitter in the brain, depend on the level of zinc. Zinc is involved in the maintenance of pyridoxal phosphate concentrations by the activation of pyridoxal kinase. Pyridoxal kinase is important for decarboxylation, and the lack of this enzyme results in reduced brain GABA levels. The level of GABA tends to be lower in the cerebrospinal fluid (CSF) during seizures (7-9). In addition, zinc appears to significantly reduce the severity of illness and the duration of fever in children with pneumonia and diarrhea by stimulating the activation of immune enhancing T-cells (5, 6, 10). A possible role of zinc deficiency in provoking FS has been reported in a few studies (11-13) but it is still unclear whether prescribing zinc supplements can prevent FS. The following study was designed in an attempt to answer this question.

Materials & Methods

We conducted a randomized, placebo-controlled trial, and recruited 100 children (50 in the case group and 50 in the control group) who were admitted to the Tabriz Children's Hospital with simple FS in 2009. Children above 4 years or below 1 years of age were excluded. Written informed consent was obtained from the parents, and fasting blood samples were obtained at 8 AM in order to measure serum zinc levels. The case group received 1mg/kg/day of zinc in the form of syrup of zinc sulfate, and the control group received placebo. Both groups were followed up for 1 year for episodes of febrile illnesses and recurrence of FS. At the end of the study, serum zinc levels were measured. The study protocol was approved by the local ethics committee. The data were analyzed using the SPSS version 16 for Windows software package (IBM Corporation, Armonk, NY, USA). The statistical procedures used to analyze the data included the chi-square test, t-test, and Pearson's correlation. Quantitative variables were presented as mean±SD values, and qualitative variables were presented as percentage values. The differences between the groups were considered significant when p-values were less than 0.05.

Results

A total of 60 boys and 40 girls with a mean age of 2.14 ± 0.96 years were studied. There was no statistical difference in the serum zinc levels between the 2 genders ($p=0.683$). No relationship was found between the serum zinc levels and temperature, weight, or family history of FS. A direct linear relationships were found between age and height with respect to serum zinc levels ($P<0.001$). The case group consisted of, 29 boys (58%) and 21 girls (42%) with a mean age of 2.06 ± 0.83 years, and the control group consisted of, 31 boys (62%) and 19 girls (38%) with a mean age of 2.22 ± 1.04 years. The 2 groups did not show statistically significant differences in age ($P=0.405$) and gender ($P=0.683$). The mean durations of the seizures were 4.83 ± 4.27 and 3.76 ± 3.97 min in the case and control groups, respectively ($P=0.203$). The case and control groups did not show significant differences in height (84.94 ± 8.50 vs. 85.59 ± 11.40 , respectively: $P=0.753$) and weight (11.73 ± 2.68 vs. 12.30 ± 3.24 , respectively: $P=0.341$). Table 1 shows the serum zinc levels and recurrence rates of FS in the 2 groups. At the beginning of the study serum zinc levels in the case (69.88 ± 10.81) and control (70.44 ± 8.77) groups were similar ($P=0.777$). Eight children (16%) in the case group and 8 in the control group experienced recurrent FS. An inverse relationship was found between febrile diseases and serum zinc levels. In other words, the occurrence of febrile diseases decreased with increase in serum zinc levels.

Discussion

Recurrence is observed in almost one-third of the children with simple FS. Among these children, there is a 50% possibility of recurrence within the first 6 months; 90% possibility within the first year; and 75% possibility within the first 2 years (14, 15). In our study, 16% of the children experienced recurrence of FS within a year. Many studies have evaluated prophylactic treatment methods of FS and prophylactic treatment with anti-seizure medications such as Phenobarbital has been suggested (16). In a few studies, prophylactic treatment for iron deficiency has been recommended (17, 18). The results of the present study showed that the use of zinc in supplemental doses did not prevent the recurrence of FS. A number of studies have been conducted to evaluate

the role of zinc in the occurrence of FS. Papierkowski et al. conducted a study on 18 children with FS and 15 healthy children. They observed that the levels of zinc and magnesium in the serum and CSF were lower in the children with FS than in those who were healthy (19). Mahyar et al. observed decreased serum selenium levels in children with FS (20). Burhanoglu et al. reported that the average serum levels of zinc in children afflicted with FS were lower than those in healthy children (7). A study by Gündüzet et al. on 102 children with FS indicated that the serum zinc levels in the FS group were significantly lower than those in the control group (12). Tutuncuglu et al. reported that serum zinc levels in children with FS were considerably lower than those in the control group (21). In another recent study published in 2008, Mollah examined the levels of zinc in the serum and CSF of children with FS. He observed that zinc levels in both the serum and CSF were significantly low (13, 22). On the basis of this finding, he suggested that prescribing zinc supplements might prevent FS. Kumar et al. also observed that serum zinc levels were low in FS patients (23). Schmiegelow et al. reported that GABA levels

were lower in the CSF of patients with infectious febrile disease (24). Mutations in the gene encoding the gamma 2 subunit of the GABA type A receptor have also been reported to cause lower levels of GABA in the brain, this may lower the seizure threshold (25).

In conclusion, the results of the present study showed that zinc therapy with supplemental doses (1mg/kg/day) reduced the rate of occurrence of febrile illnesses but did not prevent the recurrence of FS. We recommend that trials should be conducted using higher doses of zinc, especially in children with uncontrolled epileptic seizures.

Acknowledgment

The authors of this study acknowledge the Pediatric Health Research Center of Tabriz University of Medical Sciences for providing financial support.

Financial Disclosure

None declared.

Funding/Support

None declared.

Table 1: Comparison of Serum Zinc Levels and the Recurrence of Febrile Seizures in the Case and Control Groups.

Serum Zinc Levels	Groups		P value
	Case	Control	
Serum zinc levels, µg/dL, mean ± SD			
At the beginning of the study	69.88 ± 10.81	70.44 ± 8.77	0.777
At the end of the study	91.12 ± 7.06	73.06 ± 7.75	0.000
Recurrence of FS*, %	16	16	1.000

*FS, febrile seizure

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